## REMARKS

Claims 1-21 and 23-26 are pending in this application. Claims 1 and 12 are the only pending independent claims.

Claim 1 is directed to a method for functionally connecting portions of certain types of vertebrate nervous systems using a certain fibrin glue mixture comprising a growth factor, fibrinogen, aprotinin and divalent calcium ions (hereinafter the "fibrin glue mixture"). The method comprises bringing close to each other a portion of the peripheral nervous system and a portion of either the central nervous system or the peripheral nervous system, applying to the gap between the two portions the fibrin glue mixture, and suturing or anastomosing the two portions to be connected.

Claim 12 is directed to a method for functionally reconnecting an avulsed cervical root (a portion of the peripheral nervous system) to the spinal cord (a portion of the central nervous system) of a vertebrate using the fibrin glue mixture, by bringing the avulsed cervical root close to the spinal cord, applying the fibrin glue mixture to the gap between them, and forming an attachment between them.

Thus, in general, both of the independent claims are directed to connecting or reconnecting nerves or the like of the peripheral nervous system to the spinal cord or another portion of the central nervous system or to another peripheral nerve or other portion of the peripheral nervous system. The method claims are not directed to connecting together different portions of the central nervous system to each other. This is an important distinction.

As explained in the Remarks portion of the Amendment filed December 29, 2008 and Dr. Cheng's First Declaration, Dr. Henrich Cheng is the same Dr. Henrich Cheng who is the primary or first-named inventor in Cheng et al. (Dr. Cheng's First Declaration, paragraph 5). Thus, better than anyone, Dr. Cheng can clearly distinguish between the present invention and the subject matter of Cheng et al. U.S. Patent 6,235,041 (hereinafter "Cheng et al."). Cheng et al. is directed to a medical device of a biocompatible material for use in the treatment for a gap or defects in the central nervous system, that is adapted to enable connection of nerve fibers of gray and white matter between the proximal end and distal end thereof in predetermined openings (see Abstract). However, the present invention (the "'530 App" in Dr. Cheng's First and Second Declarations) provides a method of functionally connecting a portion of the peripheral nervous system to a portion of the central or peripheral nervous system. A clear diagram, Fig. 1 in Dr.

Cheng's First Declaration, shows the exact positions for connection in Cheng et al. and the present application, respectively, which should be helpful to clarify the difference between the two cases. The repairs of the different types or regions of the nervous systems involved different mechanisms.

Claims 1-21 and 23-26 were rejected under 35 U.S.C. § 103(a) on the grounds of obviousness over Cheng et al. in view of Schenck et al. U.S. Patent 4,553,542 (hereinafter "Schneck"). In the Examiner's Response to Arguments section at page 2 of the Office Action, the Examiner disagreed with Applicant's position that Cheng et al. does not disclose reconnecting nerves of the peripheral nervous system with nerves of the central nervous system, and quoted the following statement from Cheng et al.'s column 1, lines 33-34: "Nerve bridges were created between the peripheral nerves and the spinal cord."

The quote does not explain Cheng et al.'s disclosure, when read and understood in its entirety. In relying on the quoted language, it appears that the Examiner may have misunderstood the invention of Cheng et al.

With reference to Dr. Cheng's Second Declaration, the invention of the present application is concerned with connecting a portion of the peripheral nervous system (without white and gray matter) to a portion of the central or peripheral nervous system is quite different from Cheng et al., who provided a medical device for use in the treatment of a gap or a defect **in the central nerve system which has gray and white matter** (such as the spinal cord) (Dr. Cheng's Second Declaration, paragraph 2). Dr. Cheng further explains in paragraph 3 of Dr. Cheng's Second Declaration that the quoted language was mistaken and that viewed in its entirety, one skilled in the art would understand that Cheng et al. used a peripheral nerve as a nerve bridge, that is, as a channel, and therefore a device, to bridge the gap or defect within the central nervous system (such as the spinal cord). The device, i.e., the peripheral nerve as a channel, was not used to connect the central nervous system to the peripheral nervous system.

In one embodiment of Cheng et al., the device connecting gaps within the central nervous system, for example the spinal cord, is a nerve fiber or bundle of nerve fibers (column 2, lines 29-34). As clearly shown in Cheng et al.'s drawings, and at column 8, lines 5-9, peripheral nerves used as implants in the spinal cord were used as a channel to bridge the gap in the spinal cord for connecting the two ends of the spinal cord. Thus, there, the device was a section of a

peripheral nerve that functioned as a channel. The nerve itself has been pulled out and leaves a hollow sheath, and that is the reason why it is called a channel.

As is further pointed out in paragraph 3 of Dr. Cheng's Second Declaration, Cheng et al. clearly explains in several locations, including its claims, that the medical device, which may be in the form of one or a bundle of specially implanted peripheral nerves in the spinal cord as a channel, is used to treat a gap or defect in the central nervous system of white and gray matter.

The statement that the Examiner quoted does not say that the subject matter of Cheng et al. is effective for treatment of nerve damage between the peripheral nerves and the spinal cord. The quoted statement means that the device (or channel) according to Cheng et al. (such as a section of a peripheral nerve in one embodiment) functioned as a bridge for connecting the two ends of the spinal cord beyond the gap. Thus, as pointed out at the top of page 3 (the last portion of paragraph 3) of Dr. Cheng's Second Declaration, Cheng et al.'s device, even in the form of a section of a peripheral nerve, was not disclosed as connecting the peripheral nervous system that is not white and gray matter, either to other portions of the peripheral nervous system or to the central nervous system that is white and gray matter.

Paragraph 4 of Dr. Cheng's Second Declaration points out that the present application is a method of functionally and directly connecting a portion of the peripheral nervous system and a portion of the central or peripheral nervous system using the fibrin glue mixture claimed in the present application. In the present application, there is no device, such as sections of peripheral nerves or nerve bundles implanted for use as a channel, in making the direct connection in the peripheral nervous system, or the nerve root or spinal root (between the peripheral nerve and the central nerve), resulting in functional repair. Because of different structures and properties between the nervous systems with (central) and without (peripheral and nerve or spinal root) white and gray matter, careful and meaningful undue experimentation, was required to invent the subject matter claimed in the present application, even in view of the disclosure of Cheng et al. relating to connecting gaps or defects in the spinal cord only.

Since Cheng et al., when fairly viewed in its entirety, would disclose to one skilled in the art only the repair of the central nervous system, and not connecting the central nervous system with the peripheral nervous system or repairing defects and making connections only within the peripheral nervous system, it would not have been obvious to such a skilled person to make such repairs and connections as claimed in the present invention, even in view of Schenck.

To the extent that Schneck discloses suturing or anastomosing portions of a nerve together, there is no suggestion, other than the Examiner's conclusion that gluing and suturing would have been obvious to allow the glue to set and form a permanent bond, to use both the fibrin glue mixture and either suturing or anastomosing together the particular portions of the peripheral nervous system or the peripheral nervous system to a portion of the central nervous system as claimed in claim 1. Thus, Schenck does not meaningfully help the lack of an effective disclosure in Cheng et al.

As previously detailed and explained in paragraph 7 of Dr. Cheng's First Declaration, Schenck taught an anasotmosis device and method for using it to join a tubular anatomical structure that is supported with the body by connective tissue and has a prepared open end to a second anatomical structure, such as blood vessels, fallopian tubes, ureters, vas deferens and outer nerve sheaths (see abstract and claim 1). The use of Schenck's encircling anastomosis device would not be useful for, and therefore is totally irrelevant to a method for connection between nerves, which are not hollow tubes. What might work for connecting nerve sheathes may not be effective in connecting nerves. Moreover, Cheng et al. and Schenck, are properly combinable, because of the different structure and functions of nerves involved in Cheng et al., compared to the anatomical structures repaired in Schenck. Even assuming only for the sake of argument that these references are properly combinable, as refuted above, the combination does not teach or suggest the presently claimed invention.

Schenck neither describes nor provides a definition of "nerves" and therefore, does not recognize any difference between the central nervous system nerves and the peripheral nervous system nerves. Further, Schenck does not provide any examples showing any success in the recovery in function after using the anastomosis device. As mentioned above, "nerves" in different regions, central vs. peripheral, have different functions and structures. Schenck neither taught nor suggested the connection between the spinal cord and a peripheral nerve (i.e., nerve root, for example) or the connection of a break of a peripheral nerve with the fibrin glue mixtures containing a growth factor of the present invention, such as aFGF. Even though the nerve sheaths were anastomosed by the device of Schenck, there was still no evidence to show that such nerve sheath repair resulted in any functional recovery.

When objectively reviewed in light of their complete disclosures, particularly in view of the explanations provided in Dr. Cheng's First and Second Declarations, the combination of Cheng et al. and Schenck does not render the invention of claims 1-11 obvious and unpatentable.

Regarding claim 12, the Examiner has taken the position that the combination of Cheng et al. and Schneck discloses connecting any portion of the nervous system of a vertebrate, including the cervical root to the spinal cord. In view of these asserted disclosures, the Examiner concluded that independent claim 12 and its dependent claims would have been obvious at the time of the invention to a person of ordinary skill in the art. Applicant respectfully, but strongly disagrees.

As noted above, independent claim 12 is more specific than claim 1, in that claim 12 is directed to functionally reconnecting an avulsed cervical root to the spinal cord, something that is clearly not shown or suggested in any way in Cheng et al. Nor is it hinted at in Schenck. Here, the particular structures involved in the claimed methods are important, and cannot be discounted. The stuctures, which either do or do not contain both white and gray matter, affect the manipulative methods and materials used in them, both with respect to claim 12, as well as to claim 1 as described above.

Much more was involved in making the present invention than mere routine experimentation of the type used to determine the optimum amount of a material to be used, as explained in Dr. Cheng's First and Second Declarations.

Reconsideration and withdrawal of the rejections and an early Notice of Allowance are respectfully requested.

If discussion of any of the issues would help advance the prosecution of this application, the Examiner is invited to contact the undersigned attorney by telephone.

Respectfully submitted,

**HENRICH CHENG**

July 14, 2009 By: _____
(Date)

**ALAN S. NADEL**
Registration No. 27,363
**PANTICH SCHWARZE BELISARIO & NADEL LLP**
One Commerce Square
2005 Market Street, Suite 2200
Philadelphia, PA 19103-7013
Telephone: 215-965-1330
**Direct Dial: 215-965-1280**
Facsimile: 215-965-1331
E-Mail: anadel@panitchlaw.com

ASN
Enclosure